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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,737	07/31/2003	Ping Gao	PC27638	3875

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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	**PAPER NUMBER**
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/632,737	GAO ET AL.	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-20,24-27 and 30* is/are pending in the application.

4a) Of the above claim(s) *7,8,11 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-6, 9-10, 12-16, 18-20, 24-27, and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-20, 24-27, and 30 are pending. Applicants have amended claims 1, 3-20, 24-27, and 30. Applicants have cancelled claims 2, 21-23, 28-29, and 31. Claims 7-8, 11, and 17 are withdrawn from consideration as being drawn to non-elected species. **Claims 1, 3-6, 9-10, 12-16, 18-20, 24-27, and 30 are under consideration in the instant office action.** Receipt and consideration of Applicants' amended claim set and remarks/arguments submitted on August 22, 2007 are acknowledged.

Moot Rejections/objections

All rejections and/or objections of claims 2, 21-23, 28-29, and 31 cited in the previous office action mailed on February 22, 2007 **are moot**, because said claims have been cancelled.

Election/Restrictions

Applicants' have not commented further on the restriction and species election originally set forth in the communication mailed on September 26, 2006.

The requirement is still deemed proper and is therefore made FINAL.

Specification

The objection to the disclosure **is withdrawn** per Applicants' amendments correcting the informalities noted in the office action mailed on February 22, 2007.

The objection to claims 3-6, 9-10, 12-16, 18-20, 24-27, and 30 **is withdrawn** per Applicants' amendments correcting the informalities noted in the office action mailed on February 22, 2007

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1, 3-6, 9-10, 12-16, 18-20, 25-27, and 30 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement **is withdrawn** per Applicants' claim amendments limiting the claims to compositions comprising celecoxib in the fill material and sodium metabisulfite as the sulfite compound.

The rejections of claims 1, 3-6, 9-10, 12-16, 18-20, 25-27, and 30 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical dosage form comprising (a) selective COX-2 inhibitor of low water solubility described by formula I in claim 21 and (b) a pharmaceutically acceptable sulfite, does not reasonably provide enablement for a pharmaceutical dosage form comprising (a) all possible selective COX-2 inhibitors of low water solubility **are withdrawn** per Applicants' claim amendments limiting the claims to compositions comprising celecoxib in the fill material and sodium metabisulfite as the sulfite compound.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

The rejections of claims 1, 3-6, 9-10, 12-16, 18-20, 25-27, and 30 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is withdrawn** per Applicants' amendments removing the indefinite language cited in the office action mailed on February 22, 2007.

Claims 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is indefinite, because it is unclear whether the trademarked surfactant LABRASOL® contained within parentheses on line 6 of the as amended claim is a required limitation of said claim. Appropriate correction and clarification are required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejections of claims 1, 3-6, 9-10, 12-16, 18-20, 25-27 under 35 U.S.C. 103(a) as being unpatentable over Black et al. (U.S. Patent No. 5,733,909) in view of Sakuma et al. (EP 0695544) **is withdrawn**, per Applicants' amendments requiring that the fill material comprises celecoxib and sodium metabisulfite.

The rejections of claims 21-24 and 30 under 35 U.S.C. 103(a) as being unpatentable over Black et al. (U.S. Patent No. 5,733,909) in view of Sakuma et al. (EP 0695544) as applied to claims 1-6, 9-10, 12-16, 18-20, and 25-29 above, and further in view of Tanida et al. (U.S. Patent

No. 6,214,378) **is withdrawn**, per Applicants' amendments requiring that the fill material comprises sodium metabisulfite.

Claims 1, 3-6, 9-10, 12-16, 18-20, 24-27 21-24 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Black et al. (U.S. Patent No. 5,733,909) in view of Sakuma et al. (EP 0695544), Tanida et al. (U.S. Patent No. 6,214,378), and Faour et al. (US 2004/0204413).

Applicant Claims

Applicants claim a pharmaceutical dosage form comprising a fill material sealed in capsule shells wherein said fill material comprises (a) celecoxib and (b) sodium metabisulfite, present in an amount sufficient to inhibit gelatin cross-linking and/or pellicle formation in the capsule shells upon storage.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Black and Sukuma were set forth on pages 10-12 of the office action mailed on February 22, 2007. The teachings of Tanida were set forth on page 15 of the office action mailed on February 22, 2007. Briefly, Black teaches oral pharmaceutical dosage forms (i.e. **hard or soft capsules**) comprising (i) stilbene **prodrugs of COX-2 inhibitors, which are selective for COX-2 over COX-1**, (ii) a fill material comprising water or miscible solvents (e.g. **propylene glycol, PEGs, ethanol**, etc.), and wherein aqueous suspensions of the invented formulations may contain the active in admixture with other excipients, such as **hydroxypropyl**

methylcellulose (HPMC), polyoxyethylene stearate, polyoxyethylene sorbitol monooleate, polyoxyethylene sorbitan monooleate (i.e. polysorbates), preservatives, coloring agents, flavoring agents, and sweetening agents (title; abstract; col. 2, lines 45-64; col. 9, lines 15-26; col. 9, line 66 through col. 10, line 10; and col. 10, lines 35-56). Briefly, Sukuma teaches that hard gelatin capsules are sometimes denatured (e.g. cross-linked) during storage under warmed conditions, which has been attributed to the presence of PEG and other compounds (e.g. triethyl citrate) and that this **denaturation may be minimized or prevented by the addition of free-radical scavengers in amounts of 0.01-5% w/w, preferably, such as, sodium sulfite, sodium hydrogensulfite, tocopherol, and ascorbic acid** (pg. 2, lines 21-33; abstract; pg. 2, lines 49-50; pg. 3, lines 8-17). Briefly, Tanida teaches pharmaceutical formulations in which an active substance is encapsulated and released in the lower gastrointestinal tract. The active substance is preferably an anti-inflammatory agent that it is a COX-2 inhibitor, such as celecoxib (col. 3, lines 12-16, 41, and 56-57). Tanida's formulations may include additives, such as vehicle, liquid agent, absorbefacient, etc. (col. 3, line 62 through col. 4, line 26), wherein suitable absorbefacients include **polyethylene glycol sodium dodecyl sulfate, sucrose fatty acid esters**, etc.

Faour teaches (i) pharmaceutical compositions comprising a COX-II inhibitor (e.g. celecoxib) and a muscle relaxant (title; abstract; claims 1 and 10) and (ii) that antioxidants include **ascorbic acid, ascorbyl palmitate, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), propyl gallate, hypophosphorous acid, sodium ascorbate, sodium bisulfite, sodium metabisulfite**, etc. [0072]. Antioxidants are agents that inhibit oxidation and are also known as free-radical scavengers.

Ascertainment of the Difference Between Scope the Prior Art and the Claims

(MPEP §2141.012)

Black lacks the teaching of pharmaceutical dosage forms comprising sodium metabisulfite. This deficiency is cured by the teachings of Faour.

Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of Black/Sukuma and Tanida, because the Black/Sukuma combination teaches capsule formulations comprising a selective COX-2 inhibitor and Tanida teaches capsule formulations wherein it is preferable to utilize a COX-2 inhibitor as an anti-inflammatory agent. A person of ordinary skill in the art would have been motivated to either substitute celecoxib for Black's invented selective COX-2 inhibitors or include celecoxib as an additional active agent because Black teaches that additional active agents may be included in the composition. Furthermore, the inclusion of an additional selective COX-2 inhibitor having a different core structure would be expected to at least yield an additive effect regarding the compositions' ability to inhibit COX-2 and therefore an ordinary skilled artisan would have had a reasonable expectation of success. Regarding the possibility of substitution of celecoxib for Black's invented COX-2 inhibitors, an ordinary skilled artisan would have had a reasonable expectation of success because celecoxib is a know selective COX-2 inhibitor. Faour's teachings demonstrate that sodium sulfite and sodium metabisulfite are functional equivalents. Thus, given Sakuma' preference for the inclusion of sulfite compounds and the fact that sodium sulfite and sodium metabisulfite are functional equivalents, it would

have been prima facie obvious to substitute sodium metabisulfite for sodium sulfite or to add sodium metabisulfite to a composition comprising sodium sulfite, because an ordinary skilled artisan would have had a reasonable expectation of success upon substitution or inclusion of sodium metabisulfite in the compositions of the combined prior art references. Regarding the inclusion of sodium metabisulfite in the fill material in addition to inclusion in the gelatin capsule, this would have been prima facie obvious because sodium metabisulfite would reasonably be expected to offset any oxidation that may denature the gelatin capsule in physical contact with the fill material contained within said capsule. Furthermore, Applicants' data does not demonstrate any surprising or unexpected results, because free radical scavengers (i.e. antioxidants), such as sodium sulfite and sodium metabisulfite, were known to prevent gelatin oxidation/denaturation. Applicants' data do not demonstrate any criticality to the presence of sodium metabisulfite only being found in the fill material as opposed to being admixed with the gelatin capsule or being both admixed with the capsule material and fill material. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Response to Arguments

Applicant's arguments with respect to claims 1, 3-6, 9-10, 12-16, 18-20, 24-27 21-24 and 30 have been considered but are moot in view of the new ground(s) of rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The provisional rejections on the ground of nonstatutory obviousness-type double patenting of (1) claims 1 and 10 as being unpatentable over claims 19-20, 23, and 26-31 of copending Application No. 10/633,102 (copending '102) and (2) claims 1and 3-6 as being unpatentable over claims 6-10 of copending Application No. 10/633,390 (copending '390) **are moot**, because copending applications 10/633,102 and 10/633,190 have been abandoned.

The provisional rejections on the ground of nonstatutory obviousness-type double patenting of claims 1, 4, 10, and 24 as being unpatentable over claims 19-20, 23, and 32-33 of copending Application No. 10/633,194 (copending '194) **is maintained** for the reasons of record

set forth in the office action mailed on February 22, 2007 and because Applicants have not traversed this rejection.

Conclusion

Claims 1, 3-6, 9-10, 12-16, 18-20, 24-27, and 30 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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